REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks and accompanying information, which place the application in condition for allowance. The Examiner is thanked for withdrawing the finality of the previous Office Action and for withdrawing the prior indefiniteness rejection.

I. STATUS OF CLAIMS

Claims 1-18 are currently pending. Claims 1-8, 13-15, and 18 are currently under consideration.

II. THE REJECTIONS UNDER 35 U.S.C. §102(b) ARE OVERCOME

Claims 1-3, 13-15, and 18 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Lang et al. (U.S. Patent No. 5,506,112; hereinafter "Lang"). Claims 4-8 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Capon et al. (U.S. Patent No. 4,965,199; hereinafter "Capon"). The rejections are respectfully traversed and will be addressed in turn.

The present invention is based in part on the surprising finding that lower amounts of factor VIII can be used in the treatment of haemophilia since it has been discovered that factor IXa has a potentiating (i.e., an enhancing) effect on factor VIII. The occurrence of factor VIII antibodies in haemophiliac patients can advantageously be reduced not only because lower amounts of factor VIII can be used but also because it has been surprisingly found that factor IXa masks the antigenic epitopes of factor VIII thereby rendering it less immunogenic in the circulation.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.,* 3 U .S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art

reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Turning first to the rejection over Lang, according to the Office Action, Lang teaches a method of adding a mixture of factor IXa and phospholipids to a sample containing factor VIII, wherein activated factor VIII forms a complex with factor IXa. Applicant respectfully traverses this rejection.

The Office Action indicates that the amendment of the claims to recite a "kit" does not overcome the rejection over Lang, and that the rejection of claims 1-3, 13-15 and 18 over Lang therefore stands. Applicants respectfully submit that this statement indicates only why the rejection allegedly applies to claim 1 - claim 1 is the only claim that references a "kit". Claims 2, 3, 13, 14, 15 and 18 doe not refer to a kit, nor do these claims depend from claim 1. Thus, the Office Action has failed to provide any basis for sustaining the rejection as to claims 2, 3, 13, 14, 15, and 18, and has failed to address Applicants' other statements regarding these claims. For this reason alone, the rejection of claims 1-3, 13-15 and 18 over Lang is incomplete and must be withdrawn in this form.

Applicants maintain that the pending claims are patentable over Lang. As previously stated, Lang teaches an assay method for determining the activity of factor VIII in a sample. The reagent that is used to determine factor VIII activity comprises factor IXαβ, factor X, calcium ions, thrombin, phospholipids and, if desired, factor XIa and factor XIIa (column 1, lines 64 to 67). A kit is also described (column 2, lines 28 to 34) as well as a method for measuring factor VIII activity (see column 3, lines 1 to 9).

In contrast, pending claim 1 recites a kit comprising two **pharmaceutical compositions**. Lang fails to teach any **pharmaceutical compositions**, let alone a kit comprising two **pharmaceutical compositions**.

Pending claim 2 recites a method of making a **pharmaceutical composition**, and pending claims 3 and 18 relate to a **pharmaceutical composition** per se. As stated above, Lang does not teach any **pharmaceutical compositions**.

Pending claims 13-15 relate to a method for **potentiating factor VIII**. As mentioned above, Lang teaches an assay method for determining the activity of factor VIII in a sample. There is no disclosure in Lang of a method for **potentiating factor VIII**. That is, while Lang relates to determining the level of activity of factor VIII in a sample, there is no teaching or

disclosure in Lang that enables one of skill in the art to then modify (enhance) the activity of factor VIII. It is this modulation or enhancement of the activity of factor VIII to which the present application relates; not the determination of an activity level.

That is, the Office Action fails to consider the preamble of any of the claims in determining the scope of the claims. In this respect, the Examiner is respectfully reminded that the present claims all relate to **pharmaceutical compositions** or methods of **potentiating factor VIII**; and the preamble recitation of the present claims must be fully considered in assessing patentability. *See, e.g., Diversitech Corp. v. Century Steps Inc.*, 850 F.2d 675, 7 U.S.P.Q.2d 1315 (Fed. Cir. 1988); *In re Tuominen*, 671, F.2d 1359, 213 U.S.P.Q. 89 (C.C.P.A. 1982); *In re Bulloch et al.*, 604 F.2d 1362, 203 U.S.P.Q. 171 (C.C.P.A. 1979); *In re Szajna et al.*, 422 F.2d 443, 164 U.S.P.Q. 632 (C.C.P.A. 1970); *In re Walles et al.*, 366 F.2d 786, 151 U.S.P.Q. 185 (C.C.P.A. 1966); *Smith v. Bousquet*; 111 F.2d 157, 45 U.S.P.Q. 347 (C.C.P.A. 1940); *Ex parte Varga*, 189 U.S.P.Q. 204 (P.O.B.A. 1973); *see also Kropa v. Robie et al.*, 187 F.2d 150, 88 U.S.P.Q. 478 (C.C.P.A. 1951). When the preamble of the present claims is fully considered, it is clear that the art fails to teach or suggest the instant invention.

In addition, the Examiner is respectfully reminded that **ALL** words in the claims must be considered in evaluating the patentability of the claims over the prior art. *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970); *see also In re Swinehart*, 169 USPQ 227 (CCPA 1971) ("point of novelty" was "transparen[cy]"; Court held that "functional" or "use" language was permissible, even at the "point of novelty" indicating that "there is nothing intrinsically wrong" with claiming by what something does); *In re Duva*, 156 USPQ 90 (CCPA 1967) (prior art rejection of aqueous solution "for depositing gold" reversed due to PTO failure to consider the "for depositing gold" recitation because "all factual differences which may be properly noted in any portion of a claim must be included within the basis for comparison with the prior art if we are to properly evaluate the difference between the invention defined in a claim and the teachings of a reference", i.e., "every portion of the … claims must be considered"). For instance, it is well-established law that where the preamble is essential to point out the claimed invention and give meaning and vitality to the claim, it is given the effect of a limitation. *See, e.g., Diversitech Corp. v. Century Steps Inc.*, 850 F.2d 675, 7 USPQ 2d 1315 (Fed. Cir. 1988); *In re Tuominen*, 671, F.2d 1359, 213 USPQ 89 (CCPA 1982); *In re Bulloch et al.*, 604 F.2d 1362, 203 USPQ 171 (CCPA 1979); *In re Szajna et al.*, 422 F.2d 443, 164 USPQ 632 (CCPA 1970); *In re Walles et*

al., 366 F.2d 786, 151 USPQ 185 (CCPA 1966); *Smith v. Bousquet*; 111 F.2d 157, 45 USPQ 347 (CCPA 1940); *Ex parte Varga*, 189 USPQ 204 (POBA. 1973); *see also Kropa v. Robie et al.*, 187 F.2d 150, 88 USPQ 478 (CCPA 1951).

Applicants respectfully submit that the term "**pharmaceutical composition**" has a well understood meaning in the art, and therefore cannot be discounted when reading the pending claims. For instance, a "**pharmaceutical compositions**" by definition, is suitable for administration to a human being. Furthermore, the term "potentiating" is well-known in the art and is readily accepted as "increasing" or "enhancing" the action of a drug or a biochemical or physiological action or effect.

Applicants can only surmise that the Office Action is again relying on column 1, lines 8-14 of Lang, which provides an **assay method** in which a mixture of factor IXa and phospholipids is added to a factor VIII containing sample, thus activating factor VIII to be assayed and whereby subsequently activated VIII forms a complex with factor IXa.

Assay methods, and **reagents used in assays**, are entirely separate from **pharmaceutical compositions** and methods of **potentiating factor VIII** using pharmaceutical compositions. To suggest otherwise, as the maintenance of the rejection over Lang does, fails to consider the preamble of the claims, as well as all of the words of the claim, in direct contrast to the case law.

It is not possible for the teaching of an assay, and reagents for use in the assay, to anticipate a pharmaceutical composition. Indeed, the section of Lang in question refers specifically to a "sample" upon which the assay is performed. In this context, the "sample" is known in the art as being material obtained and existing outside of the body. One would not utilize the term "sample" in this manner when referring to an *in vivo* assay. Thus, it is clear that Lang's assay does not take place within a subject, such that the assay reagents are not given to a subject, and therefore do not meet the definition of a "pharmaceutical composition".

Further, it certainly appears that the Examiner is confusing the expressions "thus activating factor VIII to be assayed" and "potentiating factor VIII" as used in the pending claims. Applicants respectfully submit that one of skill in the art would readily understand that the meaning of these expressions is very different. Factor VIII is a glycoprotein procofactor synthesized and released into the bloodstream by the endothelium. In the circulating blood, it is mainly bound to von Willebrand factor (vWF, also known as Factor VIII-related antigen) to form

a stable complex. Upon activation by thrombin, it dissociates from the complex to interact with factor IXa in the coagulation cascade. Accordingly, the expression "thus activating factor VIII to be assayed" in Lang refers to the activation of stable factor VIII complex by thrombin leading to dissociation. In contrast, the expression "potentiating factor VIII" as used in the pending claims refers to the surprising observation described in the present application in which the effect of factor VIII is **enhanced** in the presence of factor IXa, thereby allowing the amount of factor VIII that is used to be reduced (see the present application as filed at page 4, lines 6 to 8; page 6, lines 10 to 12; and pages 21 to 23).

Thus, a proper reading of the term "potentiating" in the present claims demonstrates that the claims 13-15 are not anticipated by the assay method described in Lang.

Thus, for all of the reasons provided above, Lang does not anticipate claims 1-3, 13-15, and 18 and the rejection must be withdrawn.

Turning now to the rejection of claims 4-8 over Capon, the Office Action asserts that Capon teaches a step where factor IXa initiates the conversion of factor X to the activated form, factor Xa, where factor VIII is currently believed to function as a cofactor and is required to enhance the activity of factor IXa, such that Capon allegedly teaches that factor VIII is capable of catalyzing the conversion of factor X to Xa in the presence of factor IXa as well as correcting the coagulation defect in plasma derived from hemophilia A affected individuals. Applicants respectfully disagree.

Applicants again assert that the Office Action fails to consider the preamble of any of the claims in determining the scope of the claims. In this respect, the Examiner is respectfully reminded that claims 4-8 all relate to **a method of treating hemophilia**. Nowhere in Capon is such a method of medical treatment described, let alone a pharmaceutical composition in which the presence of factor IXa allows the concentration of factor VIII to be reduced.

Indeed, Capon relates exclusively with methods to produce recombinant factor VIII from cells. It has been well known for years that factors IXa and VIII interact in the circulation to promote the activation of factor X, leading to the generation of thrombin, and this information can be found in many sources, including textbooks which relate to coagulation. However, it is not possible to predict from this knowledge that factor IXa would potentiate the activity of low concentrations of factor VIII, and such a finding as described in the present application has been surprising to those of skill in the art.

The Office Action relies on Figure 1 to argue that factor VIII and factor IXa both take part in the cascade reaction of surface mediated activation of blood coagulation and their concentrations will relate to each other as described in pending claim 4. Regardless of the meaning ascribed to "their concentrations will relate to each other" as used in the Office Action, Figure 1 simply describes the activation of blood coagulation, and does not show any evidence that reductions in the amount of factor VIII can be utilized in the presence of factor IXa due to the potentiation of the factor VIII present.. Thus, Capon has no impact on the novelty of the pending claims.

Therefore, Capon does not anticipate claim 4, nor dependent claims 5-8, and the rejection must therefore be withdrawn.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) are respectfully requested